(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 January 2004 (15.01.2004)

PCT

(10) International Publication Number
WO 2004/004705 A2

(51) International Patent Classification[7]: A61K 31/192, 31/167, 31/616, 31/4545, 31/341, 31/495, 45/06, 38/01, 35/20, 35/78, 31/718, 31/7016, 31/702, A61P 29/00

(21) International Application Number: PCT/GB2003/002866

(22) International Filing Date: 3 July 2003 (03.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0215532.3	3 July 2002 (03.07.2002)	GB
0217130.4	24 July 2002 (24.07.2002)	GB
0227595.6	26 November 2002 (26.11.2002)	GB
0229315.7	17 December 2002 (17.12.2002)	GB
0300052.8	3 January 2003 (03.01.2003)	GB

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette

WO 2004/004705 A2

(54) Title: PHARMACEUTICAL FORMULATIONS

(57) Abstract: Provided is a composition comprising one or more pharmaceutically active substances, a salt, and/or a protein, and/or carbohydrate, wherein the composition is capable of being dissolved or suspended in an aqueous solution to form a drink product in which the pharmaceutically active substance is suitable for storage.

PHARMACEUTICAL FORMULATIONS

FIELD OF THE INVENTION

The present invention concerns a pharmaceutical composition comprising medicinal active components, which composition can be dissolved or suspended in water to form a drink product that is suitable for storage. The composition comprises salts, proteins and/or carbohydrates to stabilise the pharmaceutical in water sufficiently for the drink product to be stored for sale in a wholesale or retail outlet or shop. The ready-to-drink formulation is advantageous, because it can be marketed as a ready made up, single dose product that can simply be drunk by the consumer with no need for the consumer to take the time and trouble to dissolve or suspend the pharmaceutical themselves. The product is fast acting and quick and easy to use, compared with existing products.

BACKGROUND OF THE INVENTION

Up-to-now medicinal active components generally have to be mixed with various additives and stabilisers to create a mixture which could be processed into powders, tablets, caplets (capsule-shaped tablets), liquid filled capsules, concentrated suspensions, syrups and tinctures.

The choice and utilisation of the appropriate binders and adhesives, disintegrating agents, fillers, lubricants, wetting agents/surfactants (galenism) is in some quarters of the industry considered an art. The research and development times for recipes in galenism are high and this influences the cost of the final product.

Further problems exist when the dose of the active ingredient is very small and has to be homogeneously distributed into the matrix of a large amount of "additives". A very homogenous distribution of the active component in a tablet recipe must be obtained and guaranteed before compressing the mixture. The coefficient of variation in the concentration of the medicinal active component from tablet-to-tablet must be very, very small.

In addition, all the added components may have a significant impact on the performance of a tablet or capsule, especially as regards bioavailability. Bioavailability is typically defined by:

'the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action'. Many so-called 'innocuous' additives and stabilisers used in the tabletting process can themselves affect the availability of the active substances for absorption.

Also, in the case of powdered active and excipient mixtures when compressed to form tablets, the tablets' hardness will influence their solubility very strongly. If a tablet is swallowed whole, the bioavailability may be influenced strongly too. The components of the mixture generally arrive in the stomach with an ill-defined particle size distribution, which adversely affects absorption.

The bioavailability of the active ingredient may also be affected in another way by the pressure applied during the tablet manufacture. Pressure generates heat that might deleteriously affect the active substances. It also disturbs the disintegration time of the tablet, consequently producing a poorer absorption rate.

Fast dissolving tablets have been designed to attempt to solve the above problems. However, such tablets require a large number of processing steps in their manufacture, and require know-how and specific additives to create a convenient 'to-the-consumer' tablet. The additives have an influence on the bioavailability and the absorption potential in the body, as discussed above. Further, the dispersion of the actives by, for example, effervescence, may result in a significant amount of the active coating the glass or container in which the dissolving tablet was dissolved. Accordingly, such tablets are still associated with a number of problems.

The possible influence of the numerous additives on the active component(s) is not as well evaluated as the medicinal active component itself. Hence, reducing these additives or avoiding them totally is important for increasing the effectiveness of the product.

This point is illustrated in package inserts which usually include a 'check before you take' message. One such message, for example, reads 'Do not take this medicine if you are allergic to any of the above mentioned ingredients'. This allergic threat may be known to the

consumer regarding the medicinal active component itself, but perhaps not for other components, as the allergic risk of many additives is not common knowledge among consumers. The safety record of such additives is patchy.

The number of additives that are declared in the package insert may be relatively large. For example, in NUROFEN® (the medicinal active component is ibuprofen) the tablet contains, in addition to the active component, fifteen other components. Paracetamol from ANADIN® contains, besides the active component, seven other substances and aspirin from ANADIN® contains five other substances.

The consumer has to swallow the tablet or capsules as a whole, or has to crush or crumble the tablets, and to disperse the (in most cases not totally soluble) tablet components in water and to drink the dispersion. During travelling or in places with poor water quality the necessary water or drink may not be available for the application of a medicine. Sometimes it is necessary to drink further amounts of water to deliver the medicine to the stomach.

If suspension or syrups are offered, a dosage using a spoon, teaspoon or a specially designed plastic spoon or device is necessary. Often after consumption of a medicine a drink is taken to remove the taste of the medicine.

There is also a problem in that the consumer sometimes does not read the package insert. In the case of an effervescent tablet the tablet must be dissolved in water before administration and not swallowed undissolved.

Sometimes it is very inconvenient for the consumer and occasionally not quite clear how to administer correctly the effervescent tablets; the package insert is ambiguous:

By way of example here are several exerts from treatment regimens:

".....Tablet is to be crushed and thoroughly dispersed in at least 120ml of drinking water; this solution is to be drunk, followed by approximately another 120ml of water".....

Comment: The procedure is definitively not standardised: what is *crushed*? To what extent? To a consumer what are 120ml? What is *thoroughly dispersed*?

".....The contents of one sachet are to be dissolved in water and swallowed"..... Comment: How do you empty the contents of a sachet quantitatively reproducibly?

".....The tablets should be either swallowed whole or dissolved in a glass of water"..... Comment: With a very high likelihood there will be a difference in the immediate bioavailability.

".....Take the medicine with a full glass of water or fruit juice. Add the liquid to the water."..... Comment: a full glass cannot be mixed correctly with the liquid.

A further two examples: (1) People are often aware that aspirin might have the potential for stomach ulceration. To reduce this likelihood people often take aspirin with milk to coat the stomach. However, the lactic acid present in the milk accentuates the natural acidity of aspirin, exacerbating this contra-indication. (2) Coffee and orange juice taken with alendronate reduces bioavailability by approximately 60%.

These examples show the more defined a medicinal component (i.e. without additives) is and the more defined the administration is, the better.

Accordingly, it is an aim of the present invention to solve the problems associated with known products. It is a further aim of the invention to provide a medicinal product in a form that is simple and straightforward for the consumer to take. Thus, the present invention aims to provide a ready-to-drink product, in which the pharmaceutical is pre-dissolved, or a product in which the pharmaceutical is ready to be dissolved in an aqueous solution, or in water, provided for this purpose as part of the product.

SUMMARY OF THE INVENTION

Thus, the present invention provides a composition comprising:

(a) one or more pharmaceutically active substances; and

(b) a salt, and/or a protein, and/or a carbohydrate;

wherein the composition is capable of being dissolved or suspended in an aqueous solution to form a drink product, in which the pharmaceutically active substance is suitable for storage.

The ready-to-drink product is advantageous, because it stabilises the pharmaceutical agent using ingredients normally present in a soft drink, rather than standard excipients, which have a number of problems as outlined above. On the whole soft drinks ingredients have an exceptional history of safety, but where a problem is known it is clearly defined e.g. "contains a source of phenylalanine" (e.g. in the case of artificial sweeteners, such as aspartame, which have contra-indications for sufferers of phenyl ketouria). Thus the ready-to-drink products of the present invention allow the consumer to choose a product with less chance of side effects and that is much more palatable than conventional products. The customer who has an allergy or suffers from another such side effect is now able to choose an alternative medicine and avoid the possibility that this could also contain a component to which he or she is allergic.

In the context of the present invention, suitable for storage means for storage in a wholesale outlet, before distribution, and/or in a retail outlet before sale to the customer. Generally, the pharmaceutically active component should be stable for many months in solution or suspension, in order for it to be suitable for such storage. The composition of the present invention is typically stable in aqueous solution under ambient conditions (less than 25°C at atmospheric pressure) for a period of 6 months or more, preferably 12 months or more, and more preferably 15 months or more. Most preferably it should be stable for 18 months or more. By stable, it is meant that 80 wt.% or more, preferably 90 wt.% or more, of the active ingredient remains unchanged as compared with the original quantity of that ingredient. Products that are dissolved on consumption by the consumer have a much lower stability. Typically, 10 wt.% of the active ingredient of such compositions decays or degrades within a period of 6 weeks or less.

The aqueous solution mentioned may be any suitable aqueous solution, including distilled and/or de-ionised water, tap water, still water, sparkling water, and any of the above with

added ingredients for stabilising the final solution/suspension or making the solution/suspension palatable.

The pharmaceuticals employed in the present invention are not especially limited. However, it is preferred that the one or more pharmaceutically active substances comprise one or more analgesics. Preferably the one or more analgesics are selected from ibuprofen and paracetamol (acetaminophen).

In a further embodiment, the present invention provides a composition comprising:

(a) one or more pharmaceutically active substances; and

(b) a salt, and/or a protein;

wherein the salt and/or the protein, and at least one of the pharmaceutically active substances, are soluble or sparingly soluble in water, and wherein the salt and/or protein are present in the composition in an amount of from 5 wt.% or less, such that the composition is capable of being dissolved in an aqueous solution to form a drink product.

Without being bound by theory, it is believed that he presence of a relatively small quantity of salt and/or protein is sufficient to render the composition stable for storage when dissolved in an aqueous solution. Known compositions which are designed for dissolution and consumption are not stable for storage, and instead comprise large quantities of salts and other excipients to aid in dissolution. For example, such products comprise large quantities of citric acid and sodium hydrogencarbonate in order to generate effervescence which aids dissolution and palatability of the product. However, these salts destabilise the pharmaceutical ingredient in these quantities, rendering the compositions unsuitable for storage in dissolved form.

Preferably the salt and/or protein is present in an amount of from 0.001-5 wt.%, more preferably from 0.001-2 wt.% and most preferably from 0.001-1 wt.%.

The pharmaceutical may be any pharmaceutical that is soluble or sparingly soluble in water, and is not otherwise limited. Preferably, the pharmaceutical comprises an analgesic, and more preferably it comprises paracetamol (acetaminophen).

The composition may comprise further additives as desired. It is especially preferred that the composition further comprises a carbohydrate. The carbohydrate may be present in the composition in an amount of from 0-20 wt.%, preferably from 0.1-20 wt.%, most preferably from 0.1-10 wt.%.

In a still further embodiment, the present invention provides a composition comprising:

(a) one or more pharmaceutically active substances; and

(b) 20 wt.% or less carbohydrate and/or 5 wt.% or less protein;

wherein at least one of the pharmaceutically active substances is capable of forming a suspension in water, such that the composition is capable of being suspended in an aqueous solution to form a drink product.

Without being bound by theory, it is believed that he presence of a relatively small quantity of carbohydrate is sufficient to render the composition stable for storage when suspended in an aqueous solution, by controlling the viscosity of the solution. As discussed above, known compositions which are designed for dissolution and consumption are not stable for storage, and instead comprise large quantities of carbohydrates and/or other excipients such as salts to aid in dissolution and suspension. Such products, in common with those for dissolvable species, often comprise large quantities of citric acid and sodium hydrogencarbonate in order to generate effervescence which aids dissolution and palatability of the product. However, these salts destabilise the pharmaceutical ingredient in these quantities, as discussed above.

The one or more pharmaceutically active substances in this embodiment of the invention are not especially limited, provided that they are capable of forming a suspension in aqueous solution. Preferably, the one or more pharmaceutical agents are selected from ibuprofen, loratadine, ranitidine, and cetirizine.

The composition may comprise further additives as desired. It is especially preferred that the composition further comprises a salt. The salt, (and the protein if present) may present in the composition in an amount of from 0-20 wt.%, preferably from 0.001-15 wt.%, more preferably 0.001-10 wt.%, and most preferably 0.001-6 wt.%.

The composition according to any of the above embodiments may comprise a salt, as already discussed. Any salt may be employed, provided that it does not adversely affect the utility of the composition. Preferably, the salt is selected from sodium chloride, sodium citrate, magnesium citrate, potassium chloride, potassium citrate, and sodium bicarbonate.

The composition according to any of the above embodiments may comprise a protein, as already discussed. Any protein may be employed, provided that it does not adversely affect the utility of the composition. Thus, the protein may be soluble, sparingly soluble, or may be capable of forming suspension, or a colloidal suspension in aqueous solution. Typically the protein is selected from a protein comprising lactoglobin, caseinate, and/or a protein derived from whey and/or soya. When whey protein is employed, the whey protein preferably comprises a whey protein extract comprising 60 wt.% or more of protein.

The composition according to any of the above embodiments may comprise a carbohydrate, as already discussed. Any carbohydrate may be employed, provided that it does not adversely affect the utility of the composition. Preferably, the carbohydrate is selected from maltodextrin, modified starch, fructo-oligosaccharides, lactose and galactose. When maltodextrin is employed, it is preferred that the maltodextrin is selected from maltodextrin with dextrose equivalent 4-8, maltodextrin with dextrose equivalent 8-12, and maltodextrin with dextrose equivalent 18-20.

As already alluded to, the present composition is particularly advantageous, since it can be readily made up into a ready-to-drink pharmaceutical product, with clear advantages to the consumer. Thus, generally the composition is formulated such that the one or more pharmaceutically active substances may be absorbed into the body via the digestive system.

Other pharmaceuticals and medicaments may be present in addition to the pharmaceutical mentioned above. Such further pharmaceuticals are not especially limited, provided that they do not interfere to the detriment of the effectiveness of the composition. The further medicine may thus be selected depending on the nature of the illness that the composition is designed to treat. Thus, in some embodiments, the composition may comprises one or more

further pharmaceutically active substances selected from antioxidants, nicotine, phospholipids, immune stimulants, agents effective against vascular disease, antihistamines, anti-obesity agents, agents effective against psoriasis, agents effective against an alcohol-induced hangover, agents effective against an anaesthesia-induced hangover, agents effective in the treatment of a cerebro vascular stroke, and agents effective in the treatment of bone disease.

In order to aid in dissolving or suspending the compositions of the present invention, the pharmaceutically active substances typically have an average particle diameter of less than 100 microns. However, larger particle sizes are possible, provided that the dissolution/suspension process is adapted accordingly. Preferably, the pharmaceutically active substances have an average particle diameter of less than 30 microns.

The composition according to the present invention may comprise further components for increasing the palatability of the ready-to-drink product. Thus, the composition may additionally comprise a simple sugar, if desired. Typically, the simple sugar is selected from lactose, galactose, glucose, fructose and any monomer sugar. The composition may further comprise flavourings, preservatives, sweetening agents, antioxidants, phospholipids, energy and/or immune stimulants, calcium and/or phytoestrogens. Such agents are well known in the soft drinks industry, and any such agents may be employed in the present compositions, provided that their effectiveness is not impaired.

The present invention further provides a method of making a composition as defined in any preceding claim, which method comprises blending the pharmaceutically active substance with the salt, and/or the protein, and/or the carbohydrate, and/or any further ingredients, and sieving the blended ingredients through a screen to form the composition. Optionally, the composition may be further processed into tablets, or other forms suitable for dissolution/suspension, if desired.

Further provided by the present invention is a drink product comprising a composition as defined in any preceding claim, which is dissolved or dispersed in aqueous solution. The drink product is a medicinal product and is stable for storage as discussed above. Generally

is in a 'one shot' dosage format. This means that when the whole drinks product is consumed, the consumer receives a standard dose of the medicament or pharmaceutical present in the drinks product. The drinks product is typically flavoured, coloured, and/or sweetened in order to give it the taste and appearance of a soft drink. The concentration of the pharmaceutical in the drink product is not especially limited, and depends on the pharmaceutical employed. Typical concentrations of pharmaceutical agent in solution range from approximately 1 μg/ml to approximately 70 mg/ml. The preferred type of product is a one 'shot' product, in which the drink can be finished in one swallow. The typical volume of drink in a single one 'shot' dose would be approximately 30 ml. Other products can be envisaged in which the volume is greater or smaller than this. The concentration of the pharmaceutical may be altered accordingly in order to ensure that a standard dose is still delivered.

The drink product of the present invention typically exhibits a pH of from 2.8-8.2. More preferably it has a pH of from 3.3-4.5 and most preferably a pH of from 3.8-4.4. This aids in stabilising the pharmaceutical ingredient, and is also desirable from a palatability viewpoint. Such pH values are well suited to the addition of fruit flavours and/or juices, which have a pH in a similar range.

The present invention also provides a method of making a drink product as defined above, comprising dissolving or suspending a composition as defined above to form an aqueous solution or suspension. The quantity of water or aqueous solution employed is not especially limited, since it is the quantity of the pharmaceutical in the composition that determines the correct standard dose. Preferably sufficient liquid should be added to substantially fully dissolve or suspend the pharmaceutically active ingredient. It is also preferred that the water, or aqueous solution, employed is heavily vortexed. This aids dissolution/suspension and allows lower quantities of additives to be employed.

The invention further provides a system for storing a medicinal product, which system comprises a container and a closure, wherein the closure comprises a compartment in which a composition may be stored separately from the contents of the container, and wherein the closure further allows the composition to be released into the container as required. The

container may be in the form of a bottle, sachet or other container suitable for holding a liquid and is preferably formed from glass or plastics material. The closure may be any form of closure, but is generally in the form of a cap or lid. The closure is preferably childproof.

In the above system, the compartment (or chamber) typically contains a composition of the present invention. However, the system is not limited to containing such compositions. Preferably, the system compartment contains one or more pharmaceutically active substances, which are unsuitable for storage in aqueous solution or in aqueous suspension.

The advantage of the system is that the composition may be stored in dry form, such that even pharmaceuticals that are inherently unstable in aqueous solution may be stored (such as aspirin). Preferably, the system comprises the correct quantity of solution in the container for dissolving/suspending the pharmaceutical, avoiding normal consumer uncertainties in such dry products that need to be dissolved on consumption.

Thus, it is preferred that the system comprises a pharmaceutical that is unstable in aqueous solution or suspension. Typically, the pharmaceutical is an analgesic. Preferably, the pharmaceutically active substance comprises aspirin.

The container may be empty if desired, in which case the consumer may fill the container with water. If necessary a level marker may be provided on the container for indicating the optimum quantity of water to add. Preferably, however, the container comprises water. Any type of water may be employed, such as distilled water, deionised water, tap water, still water and sparkling water. Preferably, the water is flavoured and/or sweetened.

It is especially preferred that the system of the present invention is adapted such that the contents of the closure compartment may be released into the container using a push mechanism. A preferred mechanism is shown in Figure 1. Preferably, the compartment or chamber is in communication with the container when the push mechanism is in the open configuration, and communication is prevented when it is in the closed position. Preferably, the compartment is isolated from the container by a frusto-conical section of the push mechanism, or a plunger, having an edge (e.g. at the widest portion of the conical section)

which abuts the casing of the closure. In the open position, the push mechanism edge sinks below the bottom edge of the closure casing to expose a gap through which the composition can fall into the communicating container.

Further provided by the present invention is a method for forming a medicinal drink in the container of a system as defined above, which method comprises:

(a) releasing the contents of the closure compartment into the container; and

(b) agitating the container to dissolve or disperse the contents of the closure compartment in the contents of the container.

The invention also provides use of a composition as defined above in the manufacture of a medicament that is effective as an analgesic. Preferably, the medicament is in the form of a drink product.

The invention will now be described in further detail by way of example only, with reference to the following Figure, in which:

Figure 1, shows the operation and components of a preferred system according to the present invention.

DESCRIPTION OF THE INVENTION

The invention refers to the solution of numerous problems inherent in the present formulations of drugs by offering a 'Ready-to-Drink' product comprising formulations of pharmaceutically active components without the addition of form-giving substances that might also have an effect on the efficacy and digestibility of the compressed tablets. Further, the 'Ready-to-Drink' products are very convenient to handle.

In particular the present invention aims to provide formulations for pharmaceutically active component using knowledge of the stabilisation of medicines in water combined with soft drinks manufacturing expertise: the use of a range of quick and short release sugars that do not provoke an insulin response in combination with a salt balance that is essentially isotonic for rapid delivery of all the components to the blood.

Accordingly, the present invention provides a composition comprising one or more pharmaceutically active substances, wherein the composition is capable of being dissolved or suspended in an aqueous solution to form a drink product.

The compositions comprising the pharmaceutically active substances are capable of being dissolved or dispersed (suspended) in water, without the normally used additives for the formulation of tablets, capsules, effervescent tablets, syrups, liquid filled capsules etc., thus forming the 'Ready-to-Drink' product.

Some pharmaceutically active substances, including aspirin, are not chemically stable in water and cannot be maintained in their active form in aqueous solution for any length of time. Therefore, it is required that these substances are kept separate from water until their use is required. It is an object of the present invention to provide a specific container integrated into the 'Ready-to-Drink' product that is capable of keeping the compositions comprising the pharmaceutically active substances separate from the aqueous solution until their consumption is required.

Accordingly the 'Ready-to-Drink' product of the present invention further comprises a drink container including a closure, wherein the closure comprises a compartment in which a liquid or dry composition can be stored separately from the contents of the container, and wherein the closure further allows the liquid or dry composition to be released into the container when desired allowing it to be dissolved or dispersed in the container contents.

A further advantage of the present invention could be that a lower amount of the active component is needed in this new application in the Ready-to-Drinks format, as it is very likely that the bioavailability will be better. The drug enters the gastro-intestinal tract in a well-defined form and absorption can occur immediately.

Such 'Ready-to-Drink' products are very convenient to the consumer and handling is very easy. No special 'glass of water' with an unspecified water-quantity or another drink must be

available. Also the consumer cannot administer the drug with an inadequate drink. Thus inconvenient dosages, using a spoon or a special device is not necessary.

Through use of the invention of the Ready-to-Drinks it is guaranteed that the correct dosage in the correct solvent (water) is swallowed and very importantly the possibility of over-dose is dramatically reduced, because it is only possible to ingest a limited amount of water per hour.

In the case of Ready-to-Drinks the rate of absorption of the medicines from the mouth into the bloodstream will be faster than, for example, a tablet as the drug is immediately ready for absorption and does not need to be released from a tablet's matrix through the process of dissolution.

Above all, these Ready-to-Drink drug formulations offer the option to conceal a bad, e.g. a bitter taste or smell by the addition of sweeteners, natural and or nature-identical flavours and flagrances. These sweeteners, natural flavours and flagrances could be chosen from a variety of components of which no side effects have been identified to date.

In addition, it is possible to use the active medicinal principle in combination with a base solvent, such as a so-called functional drink, for which no side effects have been known to date. For example, the use of a food supplement appetite suppressant hydroxycitric acid in combination with an anti-obesity drug.

In some cases a medicinally active compound is not structurally stable from a chemical point of view, and even cannot not be stored stably in the special chamber integrated into the cap. In this case it is necessary to prepare a special powder/granulate of the medicinal active component to be able to automatically weigh and dose the component with the necessary high precision into the special container integrated into the cap and/or fill the chamber in an inert atmosphere.

The Ready-to Drink system can in particular be applied to analgesics, specifically the best-known analgesics, acetaminophen (paracetamol), ibuprofen and aspirin. Accordingly the

invention is exemplified below in terms of these pharmaceutically active substances. However, it is noted that the Ready-to-Drinks system can be applied to any number of pharmaceutically active substances that are capable of being absorbed into the body via the digestive system. The present invention therefore covers formulations comprising one or more pharmaceutically active substances selected from antioxidants for assisting the fight against physiological stress, nicotine to aid the quitting of cigarettes, combinations of phospholipids for assisting liver function, immune stimulants, agents effective against vascular disease (in particular cardiovascular disease and atherosclerosis), antihistamines, anti-obesity agents, agents effective against psoriasis, agents effective against an alcohol-induced hangover, agents effective against an anaesthesia-induced hangover, agents effective in the treatment of a cerebrovascular stroke, agents effective in the treatment of bone disease such as calcium and phytoestrogens and agents that aid weight loss such as hydroxycitric acid.

In one embodiment of this invention a single analgesic (acetaminophen, aspirin or ibuprofen) is combined with simple, dimeric and/or polymeric sugars, anions and cations, flavourings, stabilisation ingredients, preservatives and sweetening agents to produce a flavoured drink with good shelf life for the convenient and immediate consumption of an analgesic to deliver fast relief from pain with an acceptable taste and mouth feel.

Preferably the analgesic is provided in a quantity for a specific medical efficacy. More preferably the product comprises 10 mg to 2000 mg of analgesic in a serving size of 10 ml to 500 ml. More preferably the serving size is 100ml to 250ml.

Typically the invention contains 100mg to 700mg of analgesic in a solution of ca 4% carbohydrates, with nature identical flavourings, in a still (non-carbonated) spring water.

The drink product preferably comprises 0.1 to 20 wt.%% carbohydrates, more preferably 1 to 7 wt.% carbohydrates. The carbohydrates can be complex carbohydrates or simple sugars. The complex carbohydrates can be oligosaccharides or polysaccharides. Preferably the complex carbohydrate is maltodextrin, derived from potato or more preferably derived from

wheat. The simple sugars can be lactose, glucose, fructose, galactose, dextrose or any monomer sugar with homologous metabolic function.

The complex carbohydrates and simple sugars can also be substituted using either a single different complex carbohydrate alone or in combination with other simple sugars. Alternatively the complex carbohydrate can be the same type but be a combination of different chain lengths e.g. one part DE (Dextrose Equivalent) 8, one part DE10-12 and one part DE18-20.

The sugars in the drink may be balanced in order that the osmolarity of the solution is isotonic.

Sugars can be added either individually or in combination. Further, artificial sweeteners such as acesulfame K or sucrolose, or a combination of artificial and natural sweeteners can be used.

Further the drink product may comprise citric acid and/or ascorbic acid as well as potassium chloride, sodium chloride and/or sodium bicarbonate.

Additionally the drink product may comprise other flavourings that would result in the product being organoleptically acceptable, depending on target consumer preference. Flavourings such as lemon emulsion or grapefruit flavour may be added. Cooling agents such as clove oil or maltol can be added at organoleptically acceptable levels to detract from the burning taste of the active pharmaceutical ingredient.

The drink product may further comprise preservatives such as potassium sorbate and/or sodium benzoate.

If preservatives are not required a form of pasteurisation can be used instead, provided none of the ingredients were heat labile. Another alternative would be dosing with 100-300ppm dimethyl dicarbonate and the mandatory quarantining of the product for 24 hours.

The ready-to-drinks product preferably comprises distilled water, spring water or mineral water, or any grade of water suitable for the manufacture of medicines. In a further embodiment an increase in the speed of absorption of the pharmaceutical active component in the Ready-to-Drinks may be facilitated by carbonating the drink, thus increasing the surface area of the liquid interacting with the absorbing surfaces of buccal epithelia cells or mucosal lining of the stomach.

Typically, a dry blend is made of all the components, excluding the preservatives and sweeteners. This blend is dispersed into water in a syrup tank to make a concentrate. A pre-dissolved solution(s) of sweetener and or preservative is then added. The concentrate is then mixed in-line with spring water and bottled aseptically on a standard neck-handling bottle filling line. Throughout, the process is GMP compliant and all ingredients used are to USP standards. In addition, during the in-line mixing stage either dimethyl carbonate (known as the Velcrin process) or ozone or hydrogen peroxide may be used to further sterilise the product or the final capped product subjected to sufficient irradiation to ensure its sterilisation.

In a further embodiment of the invention the ready-to-drinks product comprises an active pharmaceutical ingredient that is insoluble or substantially insoluble in water. In order to disperse a medicine that is insoluble in aqueous solution typically two routes are available – emulsification or use of traditional viscosity increasing agents such as guar gum and or xanthum gums. However, according to this invention the viscosity of the of the solution is raised using a combination of complex, but biologically digestible complex carbohydrates and/or proteins, that allow an effective and sustainable dispersion of the insoluble or partially insoluble pharmaceutically active ingredient to be achieved.

In one aspect of the invention the pharmaceutically active ingredient is ibuprofen. Preferably the ibuprofen is provided in a quantity for a specific medical efficacy. More preferably the drink product comprises 10 mg to 2000 mg of ibuprofen in a serving size of 10 ml to 500 ml. More preferably the serving size is 100ml to 250ml. Most preferably the drink product comprises 100 mg to 500 mg of ibuprofen.

Preferably the ibuprofen has an average particle diameter of 5 to 100 microns, more preferably 5 to 50 microns, more preferably 5 to 40 microns and most preferably 5 to 30 microns.

The bulk density of the active pharmaceutical ingredient is established by standard means (e.g. decanting the active pharmaceutical ingredient into a pre-weighed measuring container, noting the volume it occupies and calculating its mass (kg) per litre). This method is limited to active pharmaceutical ingredients with bulk densities of no more than 3 kg/litre.

Preferably the ibuprofen has a bulk density of between 0.08 and 2 kg/litre, more preferably 0.08 and 1.5 kg/litre, more preferably 0.08 and 1.0 kg/litre, more preferably 0.08 and 0.7 kg/litre, most preferably 0.08 and 0.65 kg/litre.

The bulk density of the active pharmaceutical ingredient should be equivalent to that of the complex carbohydrate and the protein ± 20%.

In this embodiment of the invention the complex carbohydrate is maltodextrin, preferably present at 0.1 to 20% w/v, more preferably 2 to 20% w/v, most preferably 4 to 20% w/v.

In a further preferred embodiment of the invention the maltodextrin is dextrose equivalent 4-8, more preferably dextrose 8-12, more preferably dextrose equivalent 10-12.

However, the complex carbohydrate can be replaced by one or a combination of indigestible complex sugars, for example fructooligosaccharides.

The protein is derived from milk or soy e.g. lactoferrin from milk or an ensemble of whey protein isolate or protein hydrolysates from soy or whey. In a preferred embodiment of the invention the protein is derived from whey.

Fractions of over 35% whey protein, more preferably over 55% whey protein, more preferably over 80% whey protein, most preferably an instantised (agglomerated to aid aqueous solubility) of more than 90% whey protein content is used.

However, the whey protein can be totally or partially replaced as an ingredient by any soluble human digestible form of protein, or peptides or combination of peptides, provided that they were soluble or formed a colloidal suspension in the finished product. These proteins can be hydrolysed or fragmented in order to aid their solubility in aqueous solution.

In a preferred embodiment of the invention the final protein concentration in the drink is 0.1 to 40 % w/v, more preferably 2-40% w/v, even more preferably 10 to 40% and most preferably 20-40% w/v.

In a preferred embodiment of the invention the Ready-to-Drink container consists of a plastic or glass bottle with preferably between 100ml and 300ml capacity and the closure comprises a lid or a cap. More preferably the bottle is an opaque PET bottle, with tamper-evident 28mm closure and label.

The Ready-to-Drinks bottles are conceived in such a way that they are easy to open by adult consumers. The cap is specially designed so that children cannot open it without having read or understood the necessary procedure of how to press and turn the cap to open the bottle ("child proof cap"). The cap might be designed such that it can only be opened once and cannot be used to reseal the medicine's container – thus preventing storage of a part dose and reducing the possibility of incorrect consumption.

In a further embodiment of the invention the ready-to-drinks product comprises an active pharmaceutical ingredient that is substantially water labile and does not remain stable in aqueous solution. Accordingly this active pharmaceutical ingredient is mixed or blended with the other ingredients as described above into a dry composition. However this dry composition is not mixed with the aqueous solution until its use is required.

In order to accommodate the dry composition a further aspect of the invention is that the closure cap of the ready to drink container may include a compartment in which the composition comprising the pharmaceutically active compound or a combination of pharmaceutically active compounds, are stored until consumption of the Ready-to-Drinks is

required. By pressing and/or turning the cap the active ingredient falls into the water This device always has to be used if the medicinal active compound is not stable from a chemical structure point of view e.g. water labile.

If this closure cap with the integrated chamber for the medicinal active component is applied it is opened by pressing and turning the special child proof cap.

The Ready-to-Drinks should either be taken before meals (that is on an empty stomach) to increase the amount of drug absorbed into the system or taken after meals (in cases where the medicinal active component may cause irritation to the gastro-intestinal tract). The proper administration time is the same as recommended for the drug in e.g. tablet format.

EXAMPLES

The present invention will now be described in more detail, by way of example only, with reference to the following specific embodiments.

Example 1 - Solution of Paracetamol in water

Final Amounts in Ready to Drink Paracetamol

Pack size 150 ml

Ingredients	grammes
Paracetamol	1.000
Citric acid	1.500
Lemon emulsion	0.150
Grapefruit flavour	0.083
Potassium sorbate	0.045
Sodium benzoate	0.023
Acesulfame K	0.054
Colourings	if needed
Carbonated water with CO2 to 2.6 vols	Up to 150
Or simply water to	Up to 150

The process for the manufacture of a still finished product requires the accurate weighing out of the materials listed above. The medicine, citric acid and acesulfame K are then pre-blended

in a double-cone blender, typically 3000 litre capacity for 10 minutes, and the resulting blend is then sieved through a fine gauge screen, typically 100 microns.

A typical batch size for the product is 10,000 litres ca 66,600 bottles. A standard 10,000 litre mixing tank with a horizontally rotating agitator (40 rpm) is filled with ca 1,000 litres of reverse osmosed water and the blended ingredients added. Stirring takes place for 20 minutes until a homogeneous suspension is present. At this time a further 7,500 litres of reverse osmosed water is added and stirring is reduced to half the previous speed for 10 minutes. During this period the preservatives are dissolved in 5 litres of water at 55 degrees Celsius. The preservatives are then added, followed by the flavourings. The volume is finally made up to 10,000 litres and stirring is switched on at 20 rpm for the remainder of the process.

In the case of a carbonated finished product. The blended product is first suspended in 1,000 litres. Mixing is as above. Next the warm preservative solution is added and then the flavourings. The volume is then made up to 1,600 litres and mixed in line with carbonated reverse osmosed water and bottle off. Dispersion is achieved in line by small constrictions every 2 metres in the stainless steel pipe-work.

The filling process occurs on standard soft-drinks industry neck-handling equipment with positive clean air flow across all points where the beverage is exposed to air. Typical achievable fill rates are 28,000 bottles per hour.

As a result of the metallic taste profile of paracetamol, grapefruit is used as one of the better masking flavourings. It is possible to substitute for other flavours that would also be organoleptically acceptable, depending on a consumer's preference. Similarly, where required the artificial sweetener could be substituted for other individual artificial sweeteners or combinations of artificial sweeteners. Sugars such as dextrose, glucose or fructose could also be added to sweeten – either individually or again in combination. If preservatives were not required a form of pasteurisation would be used instead, provided none of the ingredients were heat labile.

Example 2

This example concerns paracetamol in an isotonic solution for the treatment of alcohol induced hangover.

This product is provide in 250 ml package and delivers 1000 mg of paracetamol in an oral rehydration base which is isotonic (336 mmol/l osmolarity). The process of manufacture is as identical to that in example 1 above, however the routine necessary for artificial sweeteners is omitted as they are not present in the formulation.

Final Amounts in Ready to Drink Paracetamol in
Isotonic Solution
Pack size 250 ml

Ingredients	grammes
Paracetamol	1.000
Citric acid	0.396
Lemon emulsion	0.150
Grapefruit flavour	0.083
Potassium sorbate	0.045
Sodium benzoate	0.023
Sodium chloride	0.733
Potassium chloride	0.633
Sodium bicarbonate	0.700
Glucose	6.683
Sucrose	8.037
Fructose	0.090

The process is as in example 1 above except the medicine, citric acid, sodium chloride, potassium chloride, sodium bicarbonate, glucose, sucrose and fructose are pre-blended in a double-cone blender, typically 3000 litre capacity for 20 minutes, and the resulting blend is then sieved through a fine gauge screen, typically 100 microns.

A typical batch size for the product is 10,000 litres ca 40,000 bottles. A standard 10,000 litre mixing tank with a horizontally rotating agitator (50 rpm) is filled with ca 2,000 litres of reverse osmosed water and the blended ingredients added. Stirring takes place for 25 minutes until a homogeneous suspension is present. At this time a further 7,000 litres of reverse

osmosed water is added and stirring is reduced to half the previous speed for 10 minutes. During this period the preservatives are dissolved in 5 litres of water at 55 degrees Celsius. The preservatives are then added, followed by the flavourings. The volume is finally made up to 10,000 litres and stirring is switched on at 20 rpm for the remainder of the process.

In the case of a carbonated finished product. The blended product is first suspended in 1,000 litres. Mixing is as above. Next the warm preservative solution is added and then the flavourings. The volume is then made up to 1,600 litres and mixed in line with carbonated reverse osmosed water and bottled off. Dispersion is achieved in line by small constrictions every 2 metres in the stainless steel pipe-work.

It is possible to substitute for other flavours that would also be organoleptically acceptable, depending on a consumer's preference. Similarly, where required the artificial sweetener could be substituted for other individual artificial sweeteners or combinations of artificial sweeteners. Sugars such as dextrose, glucose or fructose could also be added to sweeten – either individually or again in combination. If preservatives were not required a form of pasteurisation would be used instead, provided none of the ingredients were heat labile. Or dosing with 100ppm of dimethyl dicarbonate and the mandatory quarantining of the product for 24 hours may be appropriate.

Example 3

One modification of the above formulation would be the substitution of glucose and sucrose with a combination of complex and simple sugars that are less insulinogenic:

Final Amounts in Ready to Drink Paracetamol in Isotonic Salts and Complex and Simple Sugars

Pack size 250 ml

Ingredients	grammes
Paracetamol	1.000
Citric acid	0.396
Lemon emulsion	0.150
Grapefruit flavour	0.083
Potassium sorbate	0.045
Sodium benzoate	0.023
Sodium chloride	0.733
Potassium chloride	0.633
Sodium bicarbonate	0.700
Maltodextrin	6.683
Acesulfame K	0.090
Lactose	8.037

Here the pre-blend would contain the medicine, citric acid, sodium chloride, potassium chloride, sodium bicarbonate, maltodextrin and lactose. Lactose could be further substituted for galactose. The manufacturing process would be as described for the isotonic version stated immediately above.

Again flavours could be omitted or substituted to meet the organoleptic requirements of the target consumer. Similarly, the artificial sweetener (acesulfame K) used to sweet in replacement for the glucose that was omitted, could itself be replaced by another artificial sweetener e.g. sucrolose or a combination of artificial or natural sweeteners. The complex carbohydrate (maltodextrin) and simple sugar (lactose) could also be substituted using either a single different complex carbohydrate alone or in combination with other simple sugars. Or the complex carbohydrate could be the same type but be a combination of different chain lengths e.g. one part DE (Dextrose Equivalent) 8, one part DE10-12 and one part DE18-20.

Example 4

It is envisaged that where the medicine is substituted with for example a poor tasting compound like ibuprofen it would also be desirable to use a method as described elsewhere in this patent to suspend the insoluble medicine and also a cooling agent to detract from the

burning taste of the product, such a cooling agent could be extract of clove oil or maltol. These would be added at levels that would provide an organoleptically acceptable beverage.

Suspension of Ibuprofen in water:

Final Amounts in Ready to Drink Ibuprofen

Pack size 150 ml

Ingredients	grammes
Ibuprofen	0.400
Citric acid	1.500
Maltodextrin	6.000
Isolated protein	4.000
Lemon emulsion	0.150
Grapefruit flavour	0.083
Potassium sorbate (preservative)	0.045
Sodium benzoate (preservative)	0.023
Acesulfame K (artificial sweetener)	0.054
Colourings	if needed
Water	Up to 150

In order to achieve an effective and sustainable dispersion of ibuprofen in water it is first necessary to blend the ibuprofen with a combination of maltodextrin (DE 10-12) and isolated protein, e.g. lactoferrin from milk or an ensemble of whey protein isolate. The medicine, the modified starch and the protein are placed in a large stainless steel container ca 2000 litres in no particular order and a nozzle capable of dispensing clean air at ca 40 PSI is mounted 40 cm above the top of the powder on a rotating propeller. The unit is sealed and the rotator spun at 40 RPM for 3 minutes and then the air is switched on at 40 PSI for a further 5 minutes. At the end of this time both the air and the rotator are switched off and the unit remains sealed for a further 10 minutes. This pre blend is then transferred to a standard 3000 litre double cone blender at blending performed at 40 RPM for 5 minutes. The citric acid and sweeteners are then added to the blender and blending starts as before for an additional 10 minutes. The blended powder is then put through the same process as above with the addition of preservatives etc applied as before.

It is possible to substitute for other flavours that would also be organoleptically acceptable, depending on a consumer's preference. Similarly, where required the artificial sweetener

could be substituted for other individual artificial sweeteners or combinations of artificial sweeteners. Sugars such as dextrose, glucose or fructose could also be added to sweeten – either individually or again in combination. If preservatives were not required a form of pasteurisation would be used instead, provided none of the ingredients were heat labile.

Example 5

Another alternative would be dosing with 100ppm dimethyl dicarbonate. For the purpose of dispersion and suspension the complex carbohydrate could be replaced by one or a combination of complex sugars, for example fructo-oligosaccharides. Similarly the protein component maybe replaced by an ensemble of peptides or combination of proteins other than those derived from milk, provided that they were soluble in the finished product.

Suspension of Ibuprofen in water:

Final Amounts in Ready to Drink Ibuprofen

Pack size 125 ml

Ingredients	Grammes
Ibuprofen	0.400
Citric acid	1.500
Maltodextrin	6.000
Isolated whey protein (instantised)	4.000
Lemon emulsion flavour	0.150
Grapefruit flavour	0.083
Potassium sorbate (preservative)	0.045
Sodium benzoate (preservative)	0.023
Acesulfame K (artificial sweetener)	0.054
Colourings	if needed
Water	Up to 125

In order to achieve an effective and sustainable dispersion of ibuprofen in water it is first necessary to blend the ibuprofen with a combination of maltodextrin (ideally DE 10-12) and isolated protein, e.g. lactoferrin from milk or an ensemble of whey protein isolate or protein hydrolysates from soy or whey.

This is a key inventive step: in order to disperse a medicine that is insoluble in aqueous solution typically two routes are available - emulsification or use of traditional viscosity increasing agents such as guar gum and or xanthum gums. Here neither are used a combination of complex, but biologically digestible complex carbohydrates and proteins are used.

The particle size of the Active Pharmaceutical Ingredient (API) is selected to be between 5 microns and 30 microns.

The bulk density of the Active Pharmaceutical Ingredient (API) is first established by standard means (e.g. decanting the API into a pre-weighed measuring containing, noting the volume it occupies and calculating its mass (kg) per litre). In this example ibuprofen of 0.6 kg/litre is suitable. This method is limited to APIs with bulk density of more than 3 kg/litre.

The bulk density of the carbohydrate polymer and the protein should be matched to the bulk density of the API.

The medicine, the modified starch and the protein are placed in a large stainless steel container ca 2000 litres in no particular order and a nozzle capable of dispensing clean air at ca 40 PSI is mounted 40 cm above the top of the powder on a rotating propeller. The unit is sealed and the rotator spun at 40 RPM for 3 minutes and then the air is switched on at 40 PSI for a further 5 minutes. At the end of this time both the air and the rotator are switched off and the unit remains sealed for a further 10 minutes. This pre blend is then transferred to a standard 3000 litre double cone blender at blending performed at 40 RPM for 5 minutes. The citric acid and sweeteners are then added to the blender and blending starts as before for an additional 10 minutes. The blended powder is then put through the same process as above with the addition of preservatives etc applied as before.

It is possible to substitute for other flavours that would also be organoleptically acceptable, depending on a consumer's preference. Similarly, where required the artificial sweetener could be substituted for other individual artificial sweeteners or combinations of artificial sweeteners. Sugars such as dextrose, glucose or fructose could also be added to sweeten –

either individually or again in combination. If preservatives were not required a form of pasteurisation would be used instead, provided none of the ingredients were heat labile. Another alternative would be dosing with 100-300ppm dimethyl dicarbonate and the mandatory quarantining of the product for 24 hours may be appropriate.

For the purpose of dispersion and suspension the complex carbohydrate could be replaced by one or a combination of indigestible complex sugars, for example fructo-oligosaccharides. Similarly the protein component maybe replaced by an ensemble of peptides or combination of proteins other than those derived from milk, provided that they were soluble or formed a colloidal suspension in the finished product.

Example 6

This example concerns an ibuprofen suspension in an isotonic solution for the treatment of alcohol-induced hangover.

This product is provide in 250ml package and delivers 400mg of ibuprofen in an oral rehydration base which is isotonic (336mmol/l osmolarity). The process of manufacture is as identical to that in example 4 above, however the routine necessary for artificial sweeteners is omitted as they are not present in the formulation.

Final Amounts in Ready to Drink Ibuprofen in Isotonic Solution

Pack size 250 ml

Ingredients	Grammes
Ibuprofen	0.400
Citric acid	0.396
Lemon emulsion	0.150
Grapefruit flavour	0.083
Potassium sorbate	0.045
Sodium benzoate	0.023
Sodium chloride	0.733
Potassium chloride	0.633
Sodium bicarbonate	0.700
Glucose	6.683
Sucrose	8.037
Fructose	0.090

The process is as in the above example except the medicine, citric acid, sodium chloride, potassium chloride, sodium bicarbonate, glucose, sucrose and fructose are subjected to the air blending as above and the resulting blend is then sieved through a fine gauge screen, typically 200 microns.

A typical batch size for the product is 10,000 litres ca 40,000 bottles. A standard 10,000 litre mixing tank with a horizontally rotating agitator (50 rpm) is filled with ca 2,000 litres of reverse osmosed water and the blended ingredients added. Stirring takes place for 25 minutes until a homogeneous suspension is present. At this time a further 7,000 litres of reverse osmosed water is added and stirring is reduced to half the previous speed for 10 minutes. During this period the preservatives are dissolved in 5 litres of water at 55 degrees Celsius. The preservatives are then added, followed by the flavourings. The volume is finally made up to 10,000 litres and stirring is switched on at 20 rpm for the remainder of the process.

It is possible to substitute for other flavours that would also be organoleptically acceptable, depending on a consumer's preference. Similarly, where required the artificial sweetener could be substituted for other individual artificial sweeteners or combinations of artificial sweeteners. Sugars such as dextrose, glucose or fructose could also be added to sweeten; either individually or again in combination, however this would clearly modify the

osmolarity of the solution and it may not longer be isotonic. If preservatives were not required a form of pasteurisation would be used instead, provided none of the ingredients were heat labile. Or dosing with 100-300ppm of dimethyl dicarbonate and the mandatory quarantining of the product for 24 hours may be appropriate.

Example 7

One modification of the above formulation would be the substitution of glucose and sucrose with a combination of complex and simple sugars that are less insulinogenic.

Final Amounts in Ready to Drink Ibuprofen in
Isotonic Salts and Complex and Simple Sugars
Pack size 250 ml

Ingredients	Grammes
Ibuprofen	0.400
Citric acid	0.396
Lemon emulsion	0.150
Grapefruit flavour	0.083
Potassium sorbate	0.045
Sodium benzoate	0.023
Sodium chloride	0.733
Potassium chloride	0.633
Sodium bicarbonate	0.700
Maltodextrin	6.683
Acesulfame K	0.090
Lactose	8.037

Here the pre-blend would contain the medicine, citric acid, sodium chloride, potassium chloride, sodium bicarbonate, maltodextrin and lactose. Lactose could be further substituted for galactose. The manufacturing process would be as described for the isotonic version stated immediately above.

Again flavours could be omitted or substituted to meet the organoleptic requirements of the target consumer, e.g. the addition of a cooling agent to detract from the burning taste of the API, such a cooling agent could be extract of clove oil or maltol. These would be added at levels that would provide an organoleptically acceptable beverage.

Similarly, the artificial sweetener (acesulfame K) used to sweet in replacement for the glucose that was omitted, could itself be replaced by another artificial sweetener e.g. sucrolose or a combination of artificial or natural sweeteners. The complex carbohydrate (maltodextrin) and simple sugar (lactose) could also be substituted using either a single different complex carbohydrate alone or in combination with other simple sugars. Or the complex carbohydrate could be the same type but be a combination of different chain lengths e.g. one part DE (Dextrose Equivalent) 8, one part DE10-12 and one part DE18-20.

Example 8 - Aspirin dosed into the cap-integrated container

Aspirin is unstable in water and could not be made as a Ready to Drink with a shelf life of any commercially useful period. Instead a cap that is both childproof and also houses a compartment has been designed, into which aspirin has been previously dispensed. During the production process the standard 28 mm wide closure is screwed onto 150 ml bottle which contains either simple water or flavoured water or sweetened and flavoured water. The process of unscrewing the novel cap from the container results in the compartment holding the medicine to open and dispense the medicine into the liquid in the container to produce the Ready to Drink medicine for immediate consumption. Figure 1 sets out the in principle design of such a cap with integrated medicine compartment.

It is possible to construct numerous different designs that result in the action of unscrewing the closed cap fitted to the container such that the integrated medicine compartment opens concomitantly.

The Production of a standardized medicinal extract from tobacco leaves to produce a drink containing nicotine at 2mg, 4mg and 8mg per bottle.

The process is as follows: pre-dried tobacco leaves are first ground to produce a series of flakes. A standard industrial kibbler is suitable. Subsequently, batch lots of 500 kg are placed in a large muslin sack, the sack sealed by drawing of a draw string and the sealed sack immersed in a 10,000 litre tank containing 5,000 litres of reverse osmosed water with sodium

metabisulphite present at 500 pm and the solution's temperature maintained at 80 degrees Celsius. An rotary agitator is present in the tank and set at 40 rpm. This is switched on for 6 minutes. At the end of this period the sack is removed from the tank, pressed to extract the balance of water from it, the tank covered and the thermostat switched off. A sample is taken and a HPLC assay run to determine the nicotine content of the solution. The tank is allowed to cool to 55 degrees at which point the solution is ready for bottling. The total volume of the solution is then adjusted using reverse osmosed water containing sodium metabisulphite at 100 ppm to the desired 2mg or 4mg or 6mg or 8mg nicotine content per 250ml. Bottling again takes place on a standard bottling line with positive pressure clean air flow over all points where the liquid is exposed to the atmosphere.

Alternative methods known in the art may be used to circumvent the microbiological risk of using natural products in this process. Examples include other preservatives or combinations of preservatives such as sodium benzoate and or potassium sorbate, flash pasteurisation or other forms of pasteurisation, or hot filling the product. Or again 100ppm of dimethyl dicarbonate may be added and the product quarantined for 24 hours.

Organoleptically the product tastes very much like black tea and for some markets it may be necessary to add either natural or artificial sweeteners or a combination of both. These are added post steeping of the leaves and in an amount and manner described elsewhere above.

The process may be further modified such that the bag is replaced with some other enclosure that allowed water to circulate through a collection of whole or fragmented leaves. Alternative temperatures and steep times may be employed to accommodate the natural variation in the starting material e.g. its water and or wax content and or fibre content all have an impact on the extraction temperature and the period of extraction.

The resulting nicotine containing water offers a good alternative to current nicotine gums and patches available to aid the quitting of cigarettes. It provides a rapid means of delivering the nicotine and also still allows the user to hold something – a cup or bottle in their hand – which is also considered an important part of the addiction.

It is also possible that other addictive drugs may be solubilised and provided in water and that a range of naturally occurring medicines derived from plant matter may be extracted in a similar manner to the above.

CLAIMS

1. A composition comprising:

(a) one or more pharmaceutically active substances; and

(b) a salt, and/or a protein, and/or a carbohydrate;

wherein the composition is capable of being dissolved or suspended in an aqueous solution to form a drink product, in which the pharmaceutically active substance is suitable for storage.

2. A composition according to claim 1, wherein the one or more pharmaceutically active substances comprise one or more analgesics.

3. A composition according to claim 2, wherein the one or more analgesics are selected from ibuprofen and acetaminophen.

4. A composition comprising:

(a) one or more pharmaceutically active substances; and

(b) a salt, and/or a protein;

wherein the salt and/or the protein, and at least one of the pharmaceutically active substances, are soluble or sparingly soluble in water, and wherein the salt and/or protein are present in the composition in an amount of 5 wt.% or less, such that the composition is capable of being dissolved in an aqueous solution to form a drink product.

5. A composition according to claim 4, wherein the one or more pharmaceutically active substances comprise paracetamol.

6. A composition according to claim 4 or claim 5, which composition further comprises a carbohydrate.

7. A composition according to any of claims 4-6, wherein the carbohydrate is present in the composition in an amount of from 0.1-20 wt.%.

8. A composition comprising:

(a) one or more pharmaceutically active substances; and

(b) 20 wt.% or less carbohydrate and/or 5 wt.% or less protein;

wherein at least one of the pharmaceutically active substances is capable of forming a suspension in water, such that the composition is capable of being suspended in an aqueous solution to form a drink product.

9. A composition according to claim 8, wherein the one or more pharmaceutically active substances are selected from ibuprofen, loratadine, ranitidine, and cetirizine.

10. A composition according to claim 8 or claim 9, which composition further comprises a salt.

11. A composition according to any of claims 8-10, wherein the salt, and/or the protein if present, is present in the composition in an amount of from 0.001-15 wt.%.

12. A composition according to any preceding claim, wherein the salt is selected from sodium chloride, sodium citrate, magnesium citrate, potassium chloride, potassium citrate, and sodium bicarbonate.

13. A composition according to any preceding claim wherein the protein is soluble, sparingly soluble, or is capable of forming suspension, or a colloidal suspension in aqueous solution.

14. A composition according to any preceding claim, wherein the protein is selected from a protein comprising lactoglobin, caseinate, and/or a protein derived from whey and/or soya.

15. A composition according to claim 14, wherein the whey protein comprises a whey protein extract comprising 60 wt.% or more of protein.

16. A composition according to any preceding claim, wherein the carbohydrate is selected from maltodextrin, modified starch, fructo-oligosaccharides, lactose and galactose.

17. A composition according to claim 16, wherein the maltodextrin is selected from maltodextrin with dextrose equivalent 4-8, maltodextrin with dextrose equivalent 8-12, and maltodextrin with dextrose equivalent 18-20.

18. A composition according to any preceding claim, wherein the composition is formulated such that the one or more pharmaceutically active substances may be absorbed into the body via the digestive system.

19. A composition according to any preceding claim, which composition comprises one or more further pharmaceutically active substances selected from antioxidants, nicotine, phospholipids, immune stimulants, agents effective against vascular disease, antihistamines, anti-obesity agents, agents effective against psoriasis, agents effective against an alcohol-induced hangover, agents effective against an anaesthesia-induced hangover, agents effective in the treatment of a cerebro vascular stroke, and agents effective in the treatment of bone disease.

20. A composition according to any preceding claim, wherein the pharmaceutically active substances have an average particle diameter of less than 100 microns.

21. A composition according to claim 20, wherein the pharmaceutically active substances have an average particle diameter of less than 30 microns.

22. A composition according to any preceding claim, wherein the composition additionally comprises a simple sugar.

23. A composition according to claim 22, wherein the simple sugar is selected from lactose, galactose, glucose, fructose and any monomer sugar.

24. A composition according to any preceding claim, wherein the composition further comprises flavourings, preservatives, sweetening agents, antioxidants, phospholipids, energy and/or immune stimulants, calcium and/or phytoestrogens.

25. A method of making a composition as defined in any preceding claim, which method comprises blending the pharmaceutically active substance with the salt, and/or the protein, and/or the carbohydrate, and/or any further ingredients, and sieving the blended ingredients through a screen to form the composition.

26. A drink product comprising a composition as defined in any preceding claim, which is dissolved or dispersed in aqueous solution.

27. A drink product according to claim 26, which drink product exhibits a pH of from 2.8-8.2.

28. A method of making a drink product as defined in claim 27, comprising dissolving or suspending a composition as defined in any of claims 1-24 to form an aqueous solution or suspension.

29. A system for storing a medicinal product, which system comprises a container and a closure, wherein the closure comprises a compartment in which a composition may be stored separately from the contents of the container, and wherein the closure further allows the composition to be released into the container as required.

30. A system according to claim 29, wherein the compartment contains a composition as described in any one of claims 1-24.

31. A system according to claim 29, wherein the compartment comprises one or more pharmaceutically active substances, which are unsuitable for storage in aqueous solution or in aqueous suspension.

32. A system according to claim 30, wherein the one or more pharmaceutically active substances comprise aspirin.

33. A system according to any of claims 29-32, wherein the container comprises water.

34. A system according to claim 33, wherein the water is flavoured and/or sweetened.

35. A system according to any of claims 29-34, wherein the contents of the cap compartment may be released into the container using a push mechanism

35. A method for forming a medicinal drink in the container of a system as defined in any of claims 29-34, which method comprises:

(a) releasing the contents of the closure compartment into the container; and

(b) agitating the container to dissolve or disperse the contents of the closure compartment in the contents of the container.

36. Use of a composition as defined in any of claims 1-24 in the manufacture of a medicament that is effective as an analgesic.

37. Use according to claim 36, wherein the medicament is in the form of a drink product.

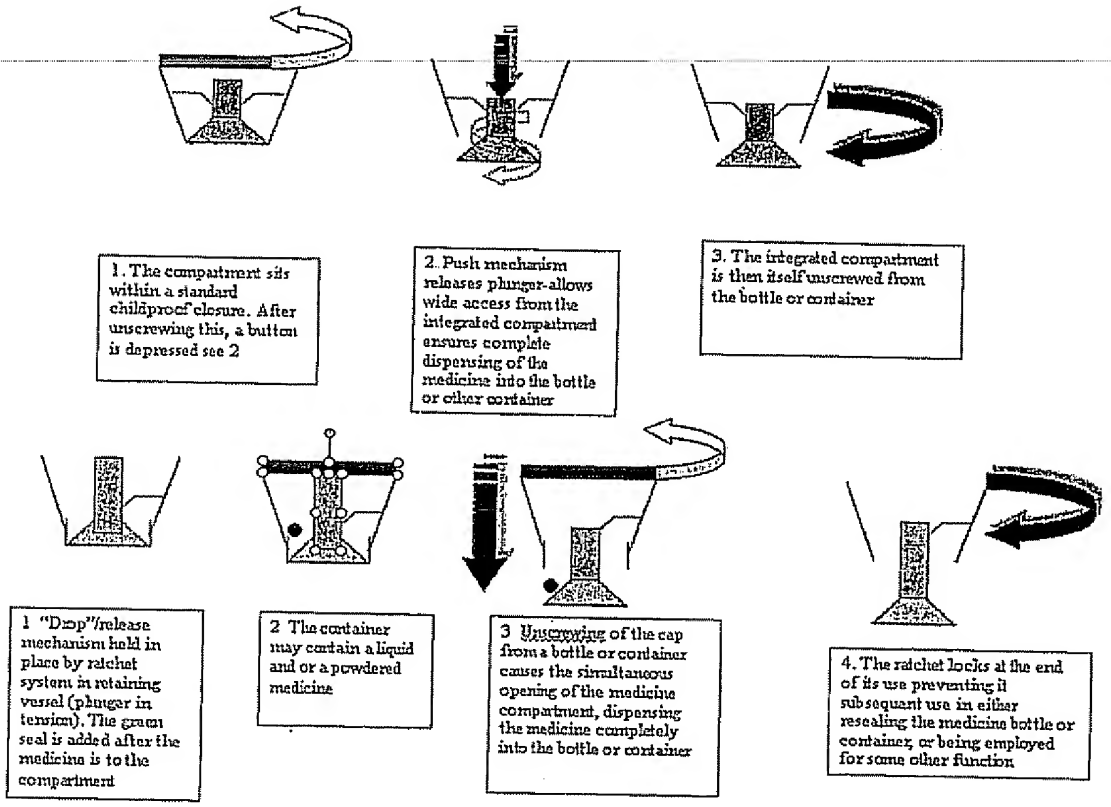
1. The compartment sits within a standard childproof closure. After unscrewing this, a button is depressed see 2
2. Push mechanism releases plunger-allows wide access from the integrated compartment ensures complete dispensing of the medicine into the bottle or other container
3. The integrated compartment is then itself unscrewed from the bottle or container
1 "Drop"/release mechanism held in place by ratchet system in retaining vessel (plunger in tension). The gram seal is added after the medicine is to the compartment
2 The container may contain a liquid and or a powdered medicine
3 Unscrewing of the cap from a bottle or container causes the simultaneous opening of the medicine compartment, dispensing the medicine completely into the bottle or container
4. The ratchet locks at the end of its use preventing it subsequant use in either resealing the medicine bottle or container, or being employed for some other function

FIGURE 1